Figure 1

A. <u>Homologous Recombination: G418 Resistance, Targeting Vector Flanked by "A" and "E"</u>
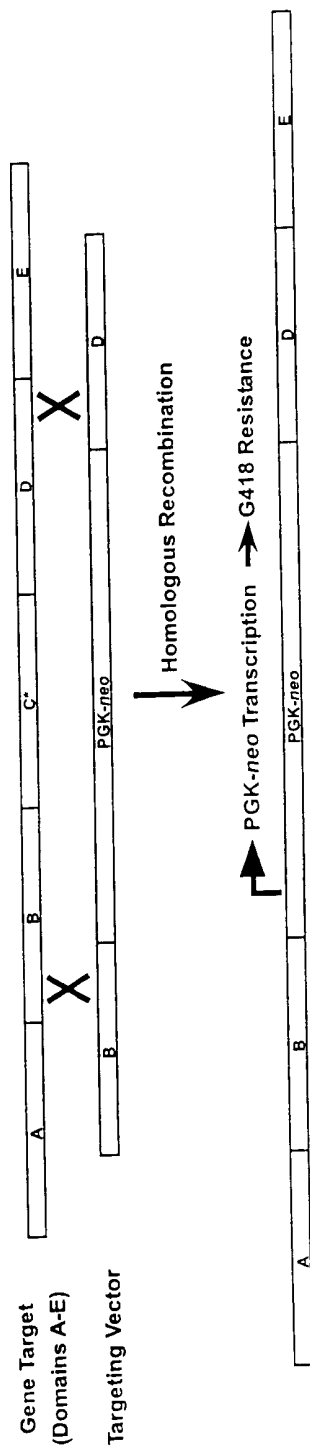
Gene Target
(Domains A-E)

Targeting Vector

Homologous Recombination

PGK-*neo* Transcription → G418 Resistance

B. <u>Random Integration: G418 Resistance, Targeting Vector Flanked by "X" and "Y"</u>

Random Genomic
Site (X,Y,Z)

Targeting Vector

Random Integration

PGK-*neo* Transcription → G418 Resistance
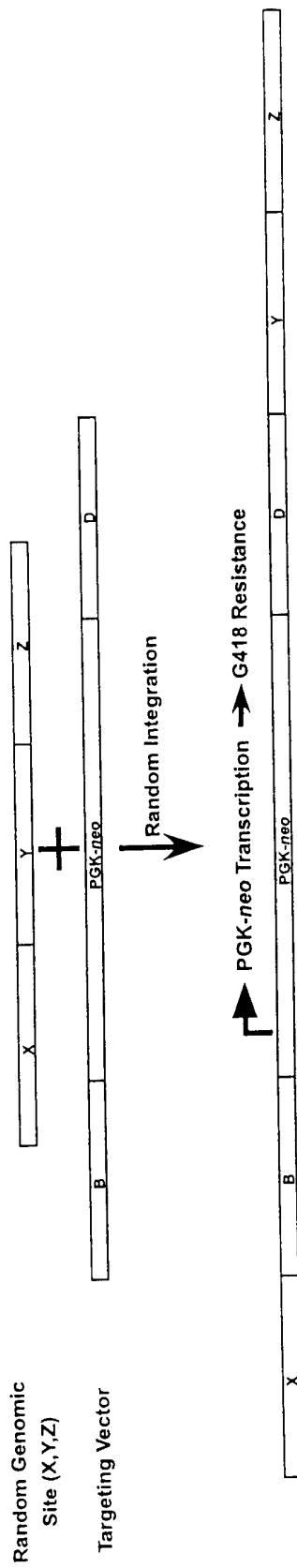
DISTINGUISH EVENTS BY SCREENING MOLECULARLY (PCR & SOUTHERN)

Figure 2

A.

Homologous Recombination: G418 Resistance + FIAU Resistance

Gene Target (Domains A-E)

Targeting Vector

Homologous Recombination

PGK-neo Transcription → G418 Resistance

Degraded → FIAU Resistance

B.
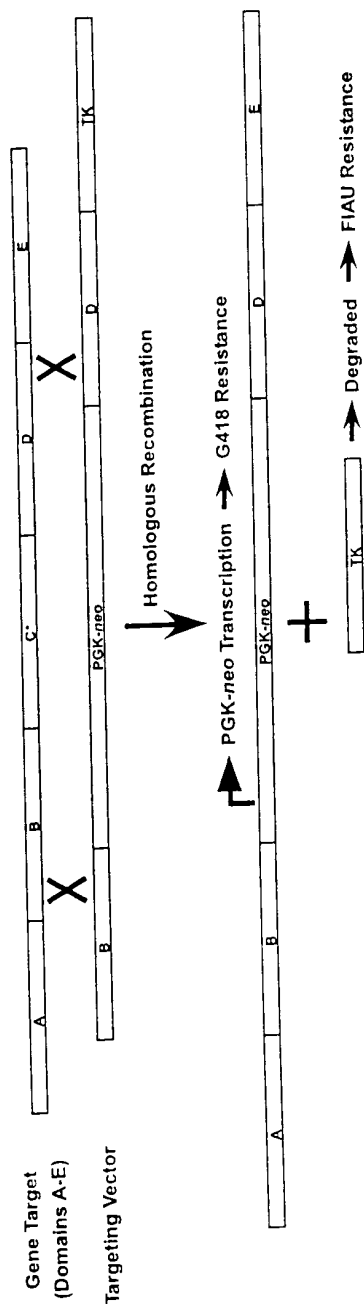
Random Integration: G418 Resistance + FIAU Sensitivity
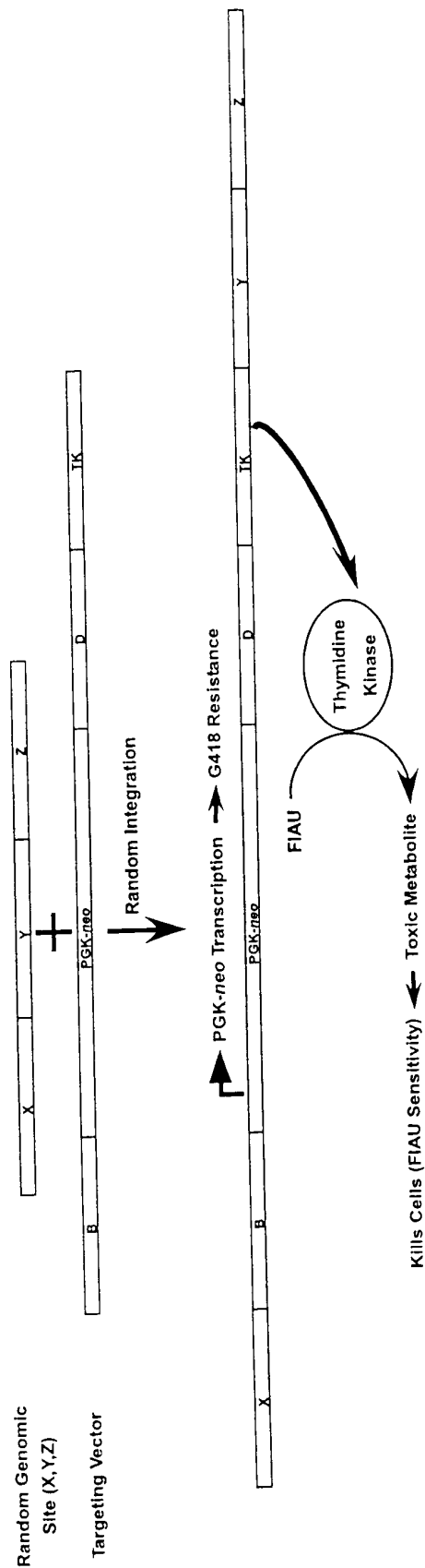
Random Genomic Site (X,Y,Z)

Targeting Vector

Random Integration

PGK-neo Transcription → G418 Resistance

Thymidine Kinase

FIAU → Toxic Metabolite

Kills Cells (FIAU Sensitivity)

Figure 3
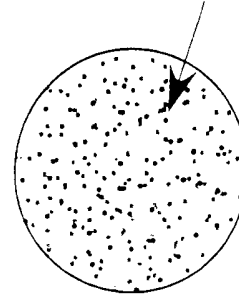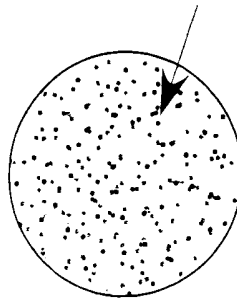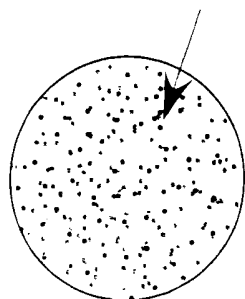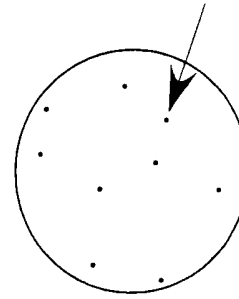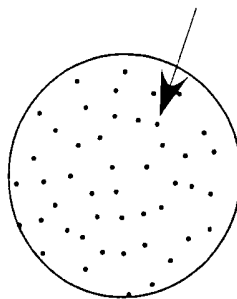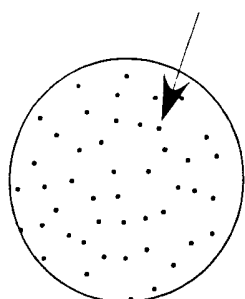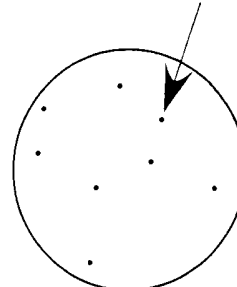
Figure 4

A. Homologous Recombination: Resistance to Selecting Drug

B. Random Integration: Sensitivity to Selecting Drug

Figure 5

C3406:

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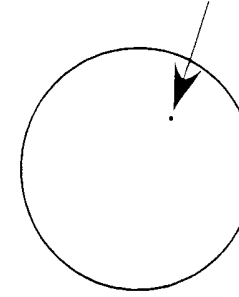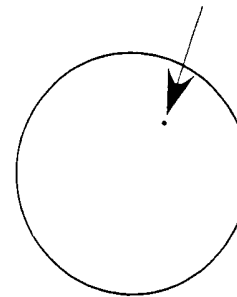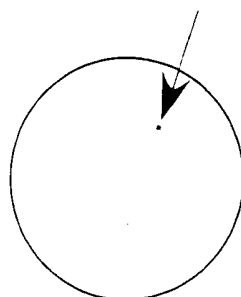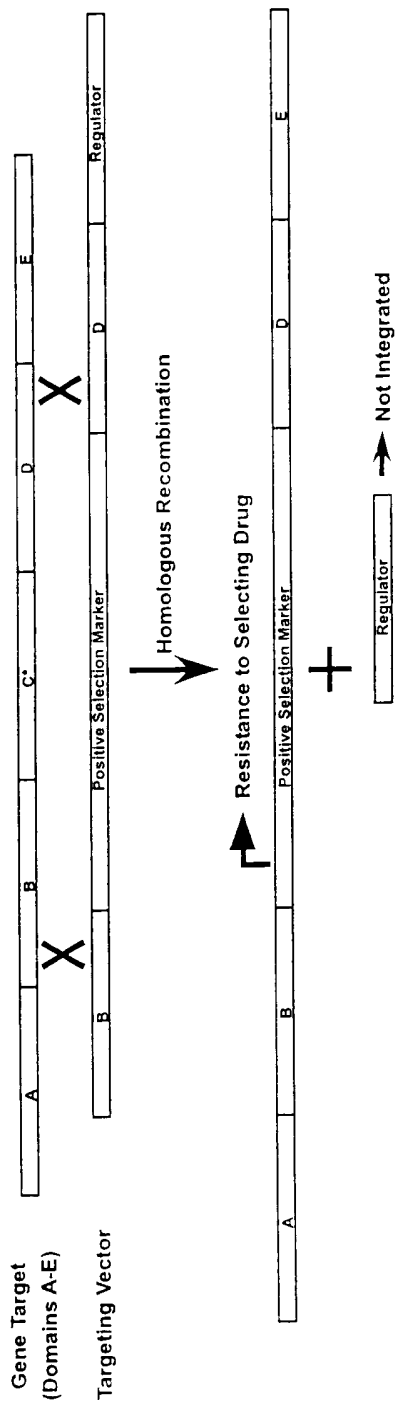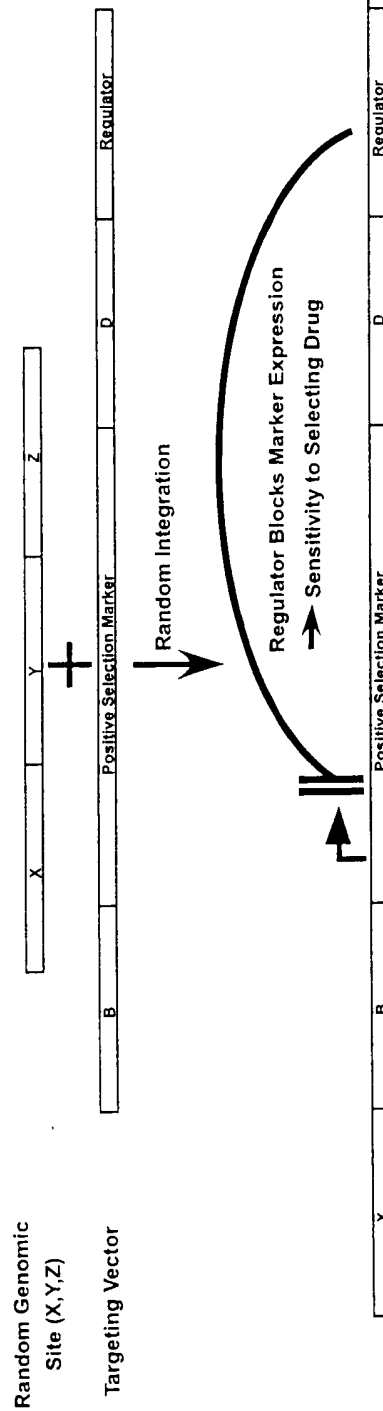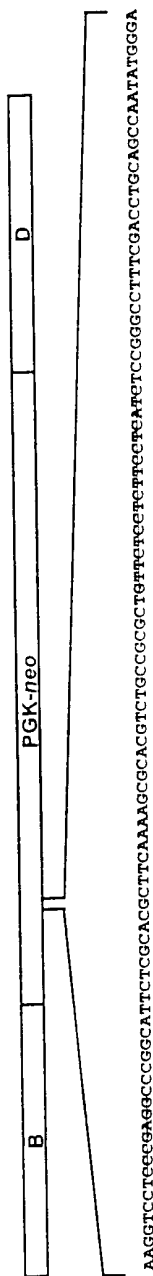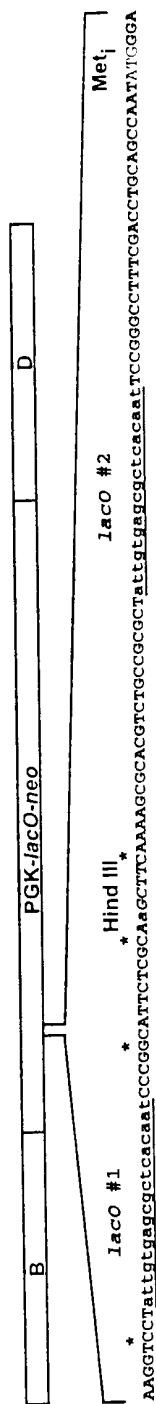
Figure 6A

B. Gene Target (Domains A-E)

A | B | C* | D | E

C. Targeting Vector: PGK-neo

B | PGK-neo | D

AAGGTCCTCCCGGAGGCCCGGCATTCTTCGCACGCTTCAAAAGCGGCACGTCTGCCGCGGCCTGTTCGCTTCCTCATCTCCGGGCCTTTCGACCTGCAGCCAATATGGGA

D. Targeting Vector: PGK-lacO-neo

B | PGK-lacO-neo | D

lacO #1

Hind III
* *
AAGGTCCTattgtgagcgctcacaatCCCGGCATTCTTCGCCAaGCTTCAAAAGCGCACGTCTGCCGCGCCTattgtgagcgctcacaatTCCGGGCCTTTCGACCTGCAGCCAATATGGGA

lacO #2

Met_i

E. Targeting Vector: PGK-lacO-neo + NLS-lacI

B | PGK-lacO-neo | D | NLS-lacI

Met_i (NLS)
GAATTCACCTGCCAGACCATGGCCAAAAAAGAAGAAGAGAAAGGTCATGAAAACCAGTAACGTTATACG

Met_i (lacI)

Figure 6 B-E

A.

Homologous Recombination: G418 Resistance

Gene Target
(Domains A-E)

Targeting Vector

Homologous Recombination

PGK-*neo* Transcription → G418 Resistance

+

NLS-*lacl* → Not Integrated

B.

Random Integration: G418 Sensitivity

Random Genomic
Site (X,Y,Z)

Targeting Vector

Random Integration

PGK-*neo* Transcription Inhibited → G418 Sensitivity

Lac
Repressor

Lac Repressor Binds *lacO* Sites

Figure 7

| Oligo #	Sequence (5' to 3')
10164	CGGAATTCACCTGCCAGACCATGCCAAAAAAGAAGAGAAAGGTCATGAAACCAGTAACGTTATACG
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10218	GCATTCTCGCAAGCTTCAAAAGCGCACGTCTGCCGCGCTATTGTGAGCGCTCACAATTCCGGGCCTTTCGACCTG
9959	TCATCAATTTCTGCAGAC
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4201	CAGGAAACAGCTATGAC

Figure 8
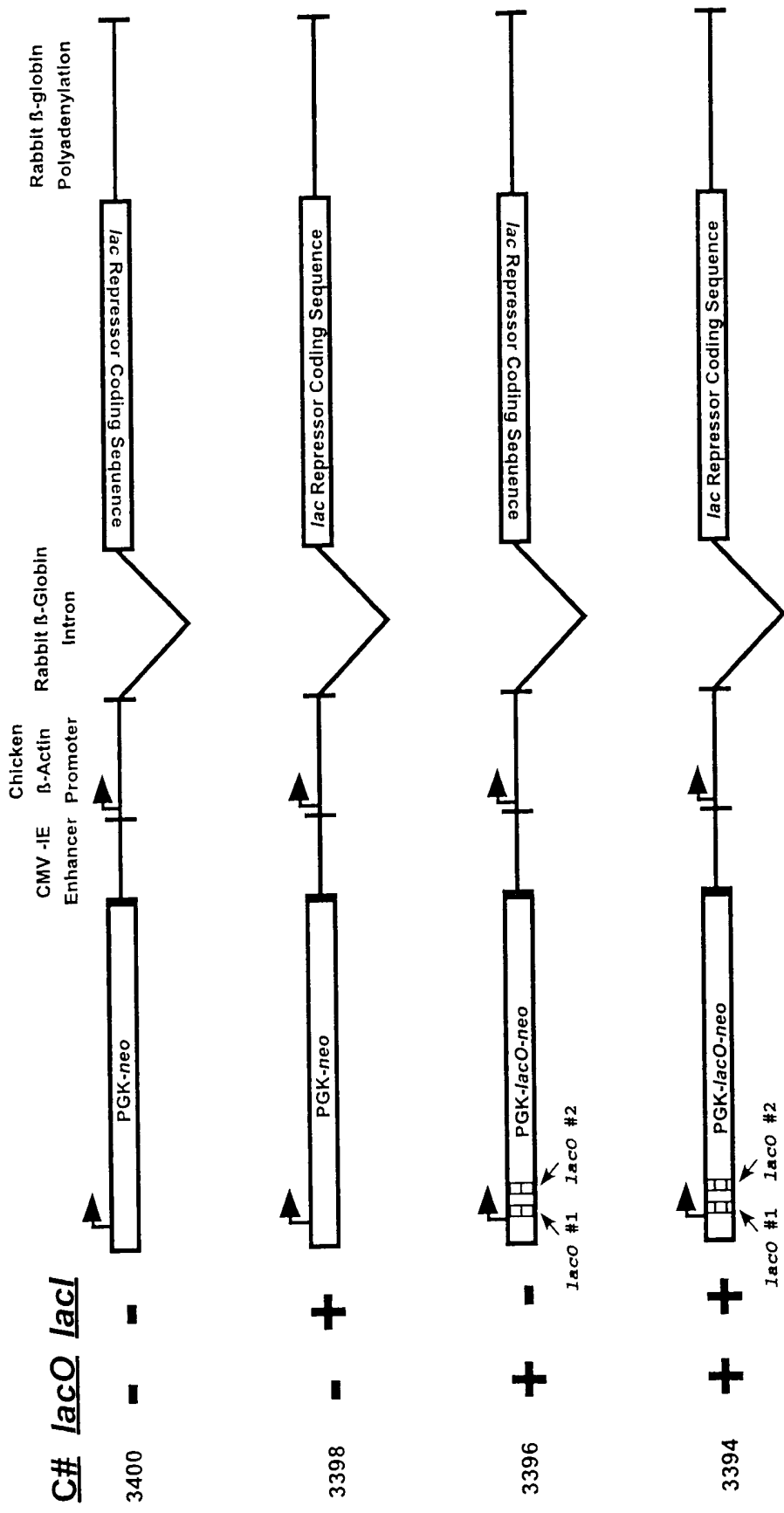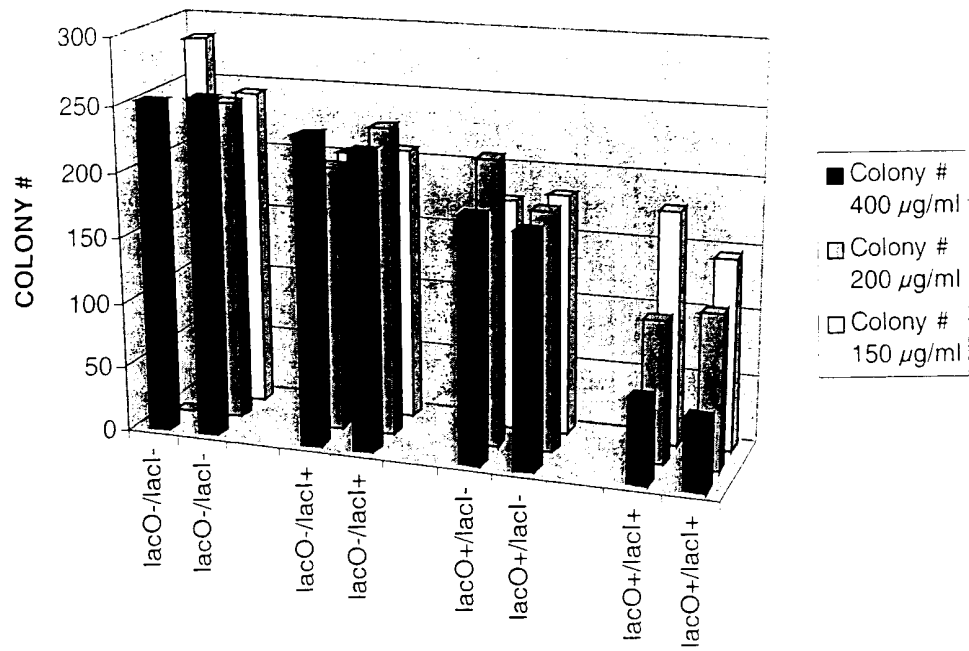
Figure 9
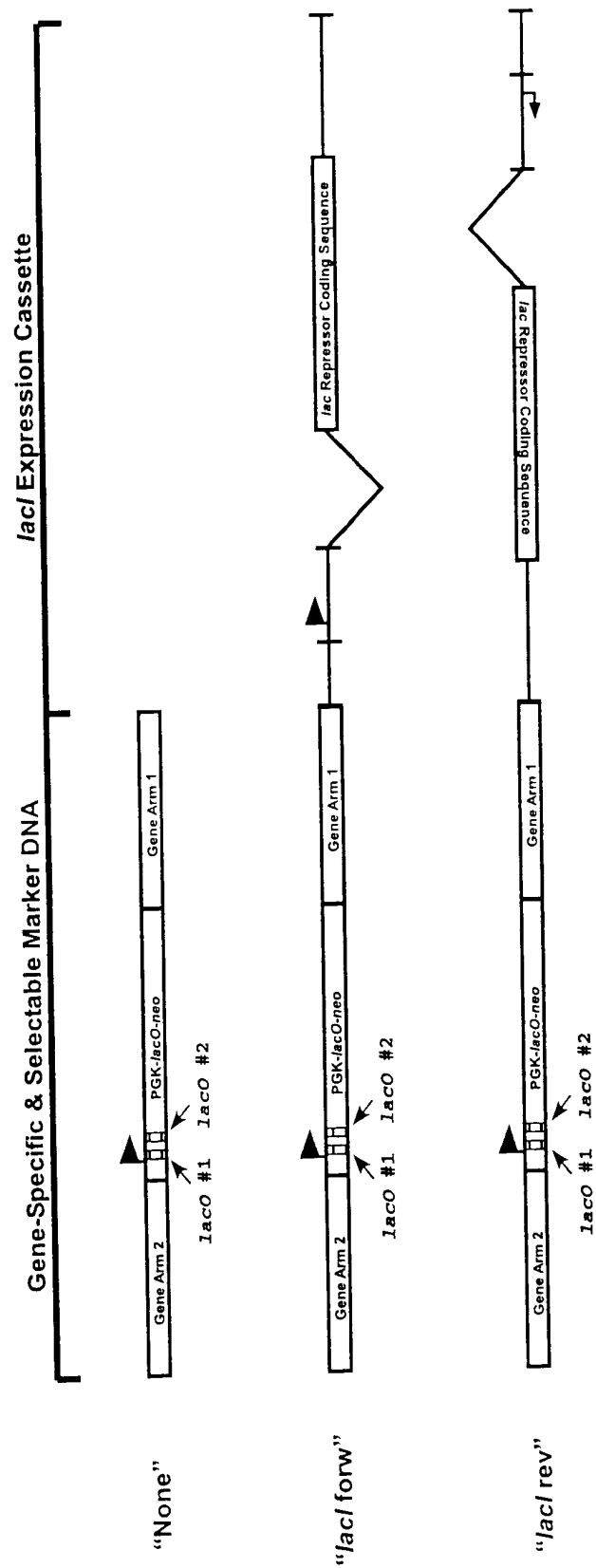
lacO + lacI REDUCE RANDOM INTEGRATION EVENTS

Figure 10

Figure 11

Homologous Recombinant Recovery Rate

Figure 12

FIGURE 13

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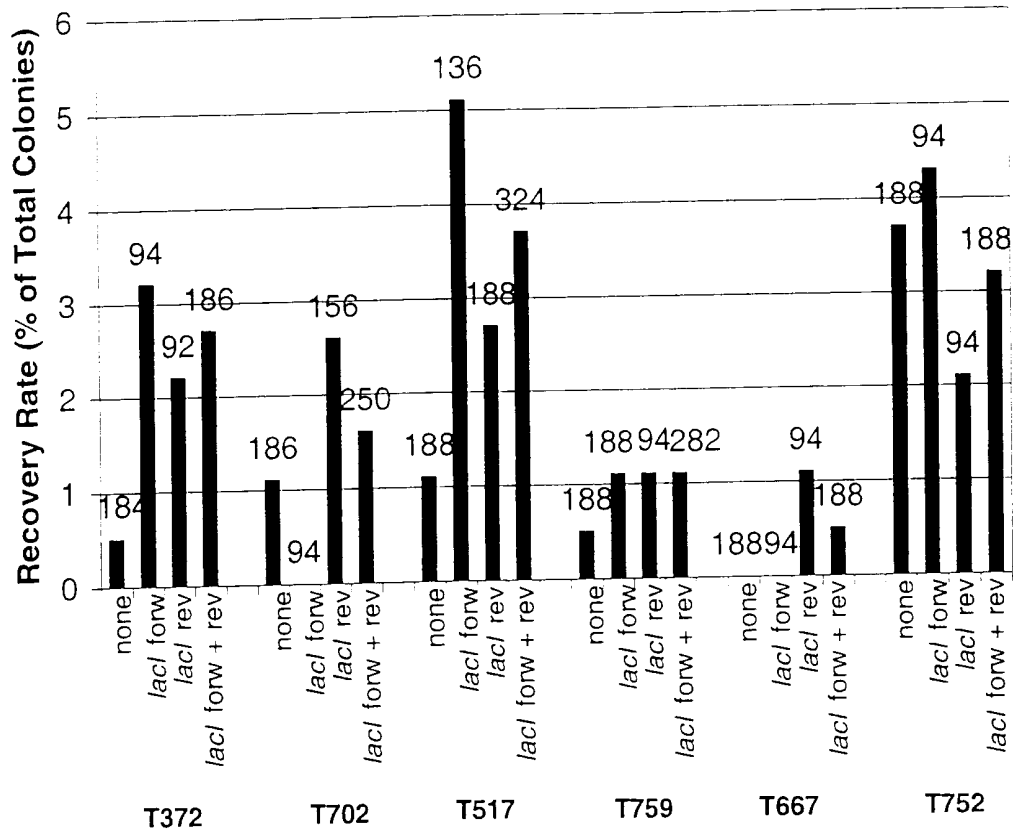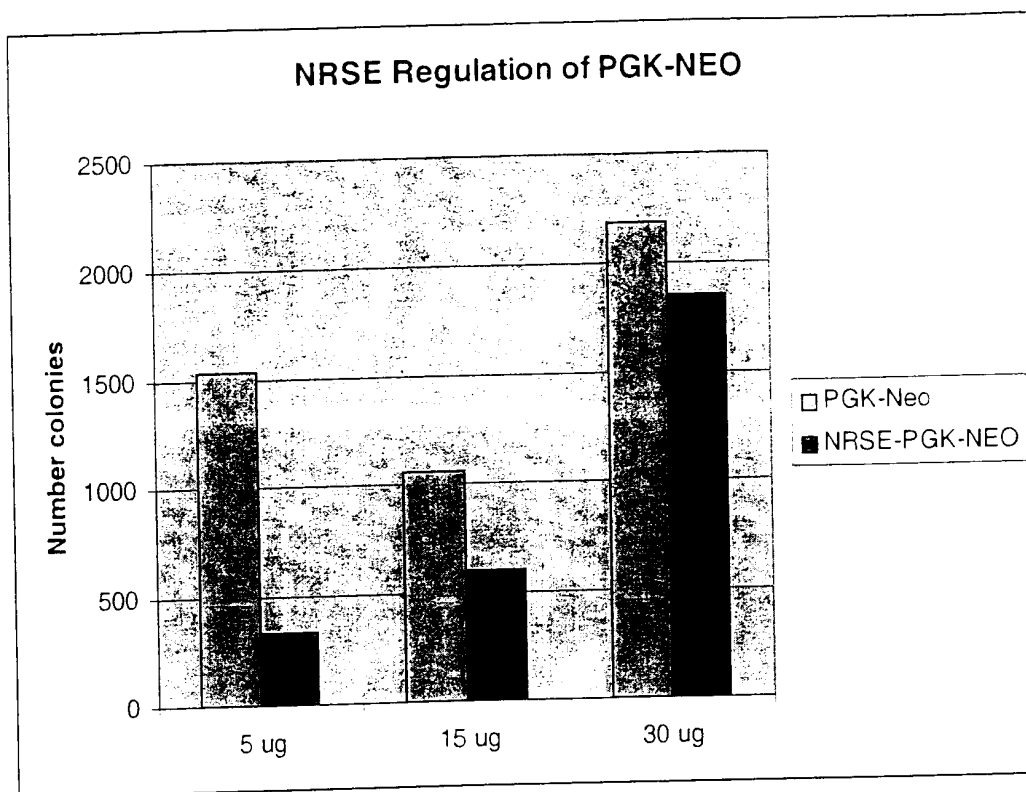
Fig.14A

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AAAAGAATAGCCCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATT
AAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACT
ACGTGAACCATCACCCAAATCAAGTTTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCG
GAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCGAACGTGGCGAGAAAG
GAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTG
CGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTAAAAGGATCTA
GGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCA
CTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCG
CGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGA
TCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAA
TACTGTTCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCC
TACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTG
TCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAAC
GGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCT
ACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCC
GGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTG
GTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATG
CTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCT
GGCCTTTTGCTGGCCTTTTGCTCACATGTAATGTGAGTTAGCTCACTCATTAGGCACCCC
AGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAAT
TTCACACAGGAAACAGCTATGACCATGATTACGCCAAGCTACGTAATACGACTCACTAG
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Fig. 14B